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EFFECTS OF METHAMPHETAMINE AND SCOPOLAMINE ON VARIABILITY OF RESPONSE LOCATION

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Methamphetamine and scopolamine were studied in monkeys responding under a multiple fixed-ratio fixed-interval schedule of reinforcement. A response on any one of six levers could satisfy the schedule requirements. Variability of response location was evaluated in terms of switches, where a switch was defined as a response on one lever followed by a response on a different lever. Under baseline conditions the fixed-ratio schedule generated a high rate of responding and a low level of variability, while the fixed-interval schedule generated a low rate of responding and a high level of variability. Both methamphetamine (0.1 to 0.5 mg/kg) and scopolamine (2.4 to 240 μg/kg) decreased overall response rate and increased variability of response location in each component of the multiple schedule with increasing doses of drug. At lower doses both drugs were found to decrease rate without affecting response variability.

Key words: response location, multiple schedule, fixed ratio, fixed interval, superstitious behavior, methamphetamine, scopolamine, lever press, monkeys

In certain situations where there are multiple operanda, variability in response location constitutes a nonrate measure of operant performance. Different levels of variability are generated by different intermittent schedules of reinforcement. For example, Boren, Moerschbaecher, and Whyte (1978) studied variability of response location under several different fixed-ratio (FR) and fixed-interval (FI) schedules of reinforcement. In that study, a monkey's response on any one of six levers could satisfy the schedule requirements. Variability of response location was evaluated in terms of switches as a percentage of the total responses, where a switch was defined as a response on one lever followed by a response on a different lever. Boren et al. found that FR schedules, ranging from FR 1 to FR 300, generated low levels of variability of response location. In contrast, FI schedules (.06 to 4 min) of comparable reinforcement frequencies were found to generate a much higher level of variability. Similar results have been obtained in pigeons (e.g., Eckerman & Lanson, 1969; Zeiler, 1968). Boren et al. concluded that variability of response location was determined by the particular characteristics of the reinforcement schedule rather than intermittence of reinforcement.

Though there have been many studies of drug effects on response rate (see review by McKearney & Barrett, 1978), relatively little is known about the effects of drugs on variability of response location. Changes in variability may be either independent of or covary with drug-induced changes in response rate. The present research was therefore designed to investigate how two drugs, methamphetamine and scopolamine, may affect both the variability of location and the rate of responding of schedule-controlled behavior. A multiple FR FI schedule of reinforcement was

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chosen for study since it controls both high (FR) and low (FI) rates of responding and both high (FI) and low (FR) levels of variability of response location.

METHOD

Subjects

One adult male patas monkey and two adult male rhesus monkeys served. The patas monkey (Monkey R) was experimentally naive at the beginning of the study; Monkey S and Monkey E had extensive histories under a variety of reinforcement schedules (e.g., see Boren et al., 1978). Each subject was maintained at about 85% of its free-feeding weight. Their diet consisted of Noyes banana-flavored food pellets, Purina Monkey Chow, fruit, and vitamins. The pellets were either earned during the experimental session or, when necessary, provided after the session. Monkey chow, fruit, and vitamins were given to each subject after the daily session. Water was continuously available.

Apparatus

The apparatus was similar to that previously described by Boren et al. (1978). Each subject was housed in a primate cage (Research Equipment Co., model LC-1103) measuring 83.6 cm by 98.2 cm by 87.4 cm. The bars were removed from one side of the cage and replaced with an aluminum panel. An array of six recessed levers (C. P. Clare Co., model C10647) were centered and aligned horizontally on the panel. The levers were spaced 7 cm apart, center to center, and were 27 cm from a perch on which the subject sat. The perch was 24 cm above the chamber floor. Each lever required a minimum force of 0.98 *N* for activation. A relay mounted behind the panel clicked when any lever was pressed. A pilot lamp (no. 1820) was mounted 4.5 cm above each lever. Below the six response levers were two additional levers (one for food and one for water reinforcement) mounted 15 and 40 cm respectively from the rear wall of the cage and 53 cm from the floor. A red pilot lamp was mounted 4.5 cm above each of these two levers. The food pellet aperture and a water tube were located between the reinforcement levers and equidistant from the middle of the panel. Only food was used as a reinforcer in the present study. In summary, response and reinforcement devices were symmetrically mounted with respect to the center of the panel such that it was possible for the subject to reach all devices with minimal movement. The reinforcement schedule was controlled by solid-state equipment. The data were recorded on counters and cumulative recorders.

Procedure

Responding was initially stabilized under a multiple FR FI schedule of food presentation (30 to 60 sessions). For Monkey S and Monkey R, the FR size was 100, while for Monkey E it was 50. A short FI value (90 sec) was used with each subject in an attempt to minimize differences in the rate of reinforcement between schedule components. The two schedule components alternated on the basis of time (17 ± 1 min). During the FR component, the lamps over the six response levers were on continuously, while during the FI component, the same lamps blinked on and off (two times per sec). A response on any one of the levers could satisfy the schedule requirements. Simultaneous responses on two different levers produced a 30-sec timeout; such responding rarely occurred following training. When the schedule requirement was met, the red lamp above the food lever came on, and a response on this lever produced a 500-mg food pellet. Each daily session terminated after a fixed number of reinforcers (200 for Monkey E and Monkey R and 250 for Monkey S) or after 4 hr, whichever occurred first.

A switch was defined as a change from one lever to another. Each time a response was made, there was an opportunity for a switch to occur. The use of a per opportunity type of measure would therefore seem necessary when comparing variability of response location either across different schedules of reinforcement which may control different rates of responding or when the manipulation of an independent variable (such as a drug) might affect the rate of responding. Switches as a percentage of the total responses was therefore chosen as a measure to evaluate the variability of response location. Thus, high variability in response location was indicated by a high percentage of switches. Rate of responding in each component also served as a dependent variable.

Methamphetamine hydrochloride was studied first in Monkeys S and E. Monkey S died

approximately 60 days after the dose-effect curves were determined. Scopolamine hydrobromide was then studied in Monkeys E and R. Methscopolamine bromide was also tested in each subject as a pharmacological control for the peripheral anticholinergic effects (e.g., dry mouth) of scopolamine. Methamphetamine was administered orally in 20 ml of a fruit-punch vehicle; scopolamine and methscopolamine were administered intramuscularly. The volume of each injection was .05 ml/kg. Doses were given in a mixed order and spaced at least six sessions apart. Drug, saline, or vehicle were all administered 5 min before the start of the session.

RESULTS

For each subject during baseline and control sessions, the FR component of the multiple schedule generated a high rate of responding, and the FI component generated relatively low rates of responding. Variability of response location also differed in each component of the multiple schedule; the FR and FI components generated low and high levels of variability, respectively. The control ranges for response rate and percent switches in each component, for Monkeys S and E, are shown in Figure 1 along with the methamphetamine dose-effect curves. Generally, in each subject, response rates decreased and response variability increased with increasing doses of drug. Note that for Monkey E, low doses of methamphetamine (e.g., .2 mg/kg) selectively decreased the rate of responding in the FR component without affecting response variability; at higher doses, however, variability increased.

The details of the multiple-schedule performance of Monkey S are shown in the top cumulative record of Figure 2. Each session started in the FR component, and the stepping pen reset with each component change. Note that switches (event pen deflections) are primarily restricted to the FI components. The effects of methamphetamine (.1 mg/kg)

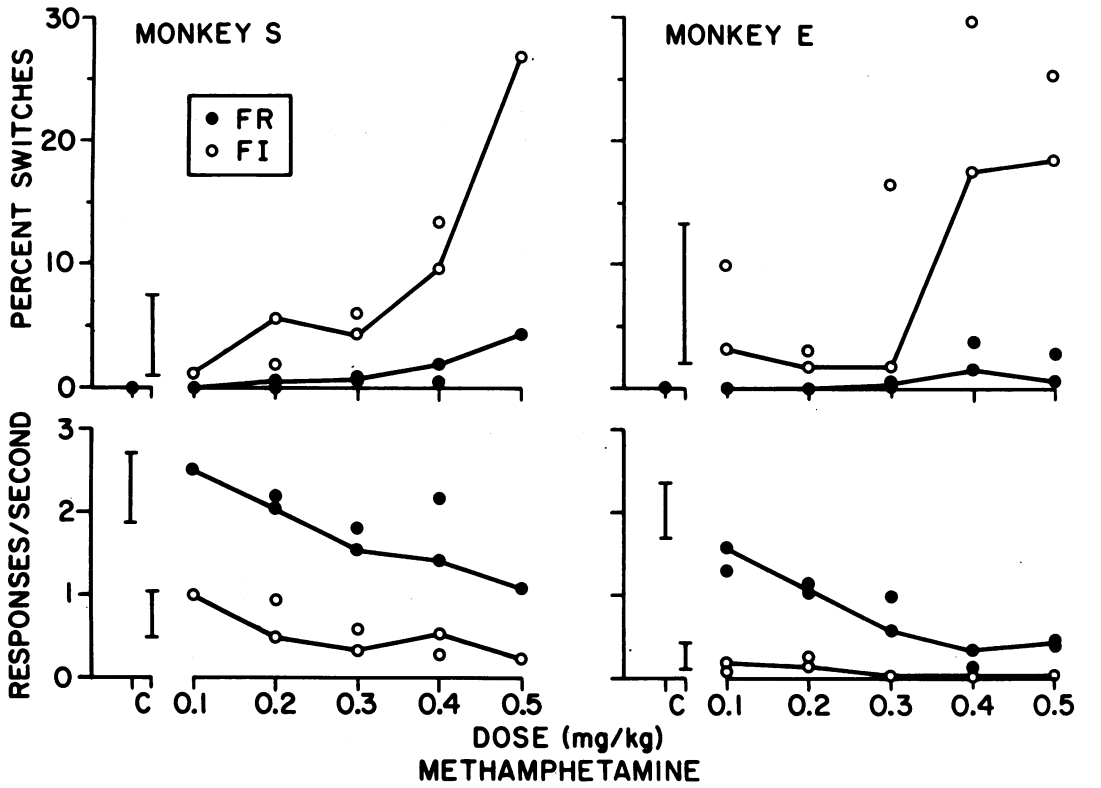

Fig. 1. Effects of varying doses of methamphetamine on response rate and switches for Monkeys S and E in each component of the mult FR FI schedule. The ranges are for 20 control sessions (C) in which the fruit-punch vehicle was administered 5 min before the start of the session. The ranges (bars or filled point) nearest to the *y*-axis are for the FR component. The points connected are those of the first determination.

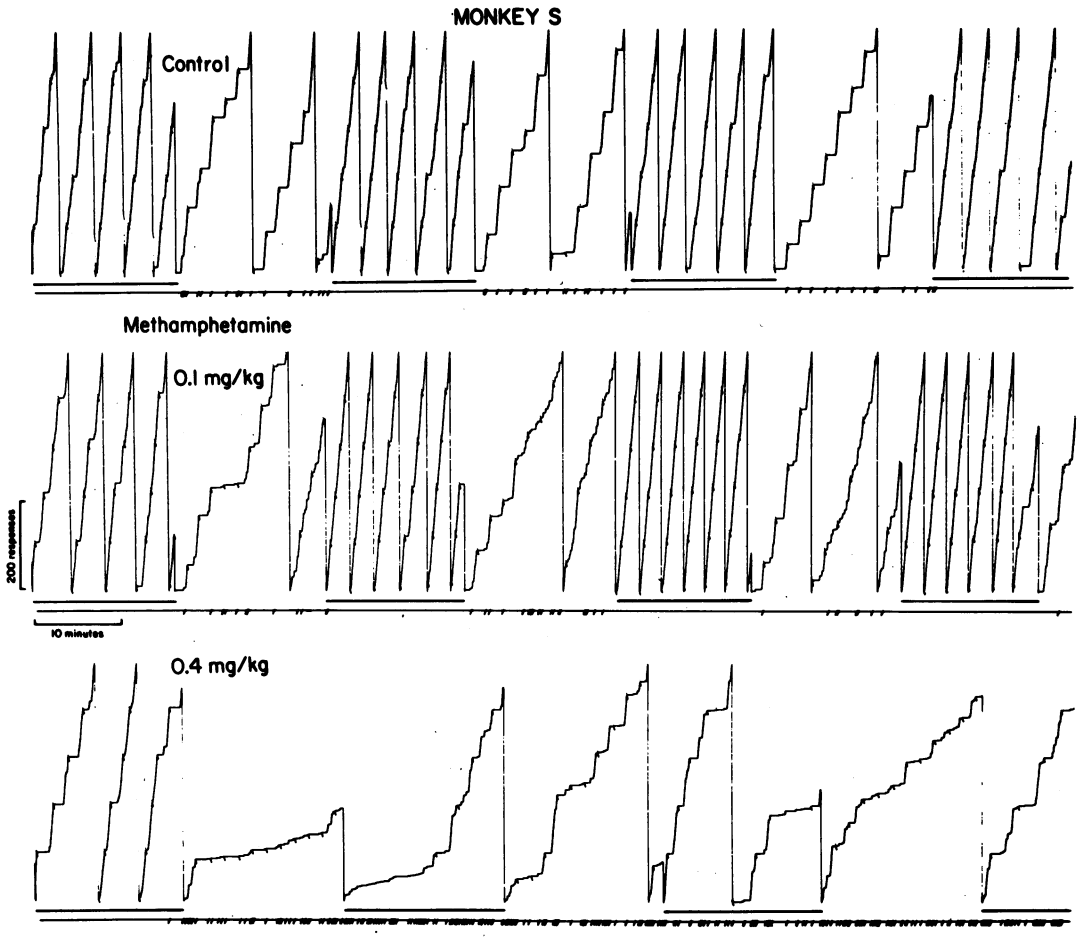

Fig. 2. Cumulative response records for Monkey S for a control session and two methamphetamine sessions under the mult FR FI schedule. The first 2 hr of each session are shown. Fixed-ratio components are indicated by a horizontal line above the event pen. The stepping pen reset with each component change. Reinforcements are indicated by the deflections of the stepping pen. Switches are indicated by deflections of the event pen.

on this performance are shown in the middle record of Figure 2. Though the overall rate of responding was not increased in either component at this dose (see Figure 1), localized rate-increasing effects did occur. For example, rates increased in both components during the third cycle of the multiple schedule. At the same time, switches in the FI component decreased. The effects of .4 mg/kg are shown in the lower record of Figure 2. At this dose, switches increased as the pattern of responding was disrupted and rates decreased in both components.

Scopolamine dose-effect curves for Monkeys R and E are shown in Figure 3. At low doses, scopolamine tended to decrease response rate without affecting switches. This selective effect occurred with Monkey R both in the FR component (10 μg/kg) and in the FI component (4.2 to 42 μg/kg). Similar effects can be seen in the FR data of Monkey E at doses of 4.2 and 10 μg/kg. At high doses in each subject, response rates generally decreased and variability of response location increased in both components of the multiple schedule.

Cumulative records for Monkey R are shown in Figure 4. Note in the saline record (top) that the FI response rate increased toward the end of the component. This patterning was characteristic of this subject's baseline performance. In comparison to saline, 24 μg/kg of scopolamine initially decreased rate in the FR component while increasing switches. As the session progressed, a more typical pattern of

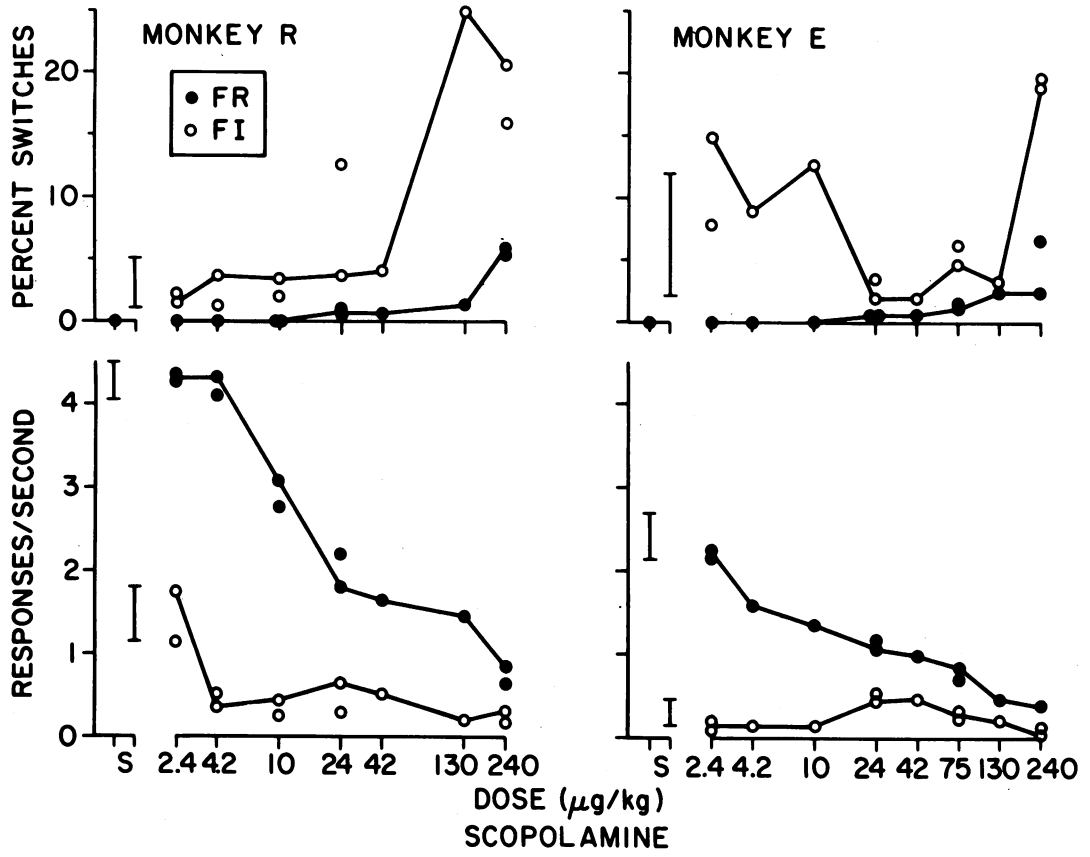

Fig. 3. Effects of varying doses of scopolamine on response rate and switches for Monkeys R and E in each component of the mult FR FI schedule. The ranges are for 14 saline (S) sessions. The ranges (bars or filled point) nearest to the *y*-axis are for the FR component. The points connected are those of the first determination.

ratio responding reappeared and switches decreased. The effects on the pattern of responding in the FI component were similar in certain respects. The greatest effects on rate occurred in the early FI components and the effects then tended to decrease as the session progressed. Switches were also decreased early in the session. At the 240 μg/kg dose of scopolamine, response rate decreased and switching increased in both components of the multiple schedule. For both subjects, methscopolamine was found to affect responding only at relatively high doses (130 to 240 μg/kg). These effects, however, were much smaller than those obtained with a comparable dose of scopolamine. The effects of methscopolamine (240 μg/kg) for Monkey R are shown in the bottom cumulative record of Figure 4. The major effect was to increase the prerun pause in the FR component. The patterning of responding generally remained intact in both components, although switching tended to decrease in the FI component.

In summary, for both methamphetamine and scopolamine, overall response rates decreased in both components of the multiple schedule with increasing doses of drug. As response rates decreased, variability of response location generally increased. At certain lower doses, however, both drugs were found to decrease rate without increasing response variability.

DISCUSSION

The rate-decreasing effects of methamphetamine and scopolamine obtained under the FR schedule are comparable to those previously reported in a variety of species, including primates (e.g., Brady, 1959; Fischman & Schuster, 1974; Johanson, 1978; McMillan, 1968). The overall rate-decreasing effects of

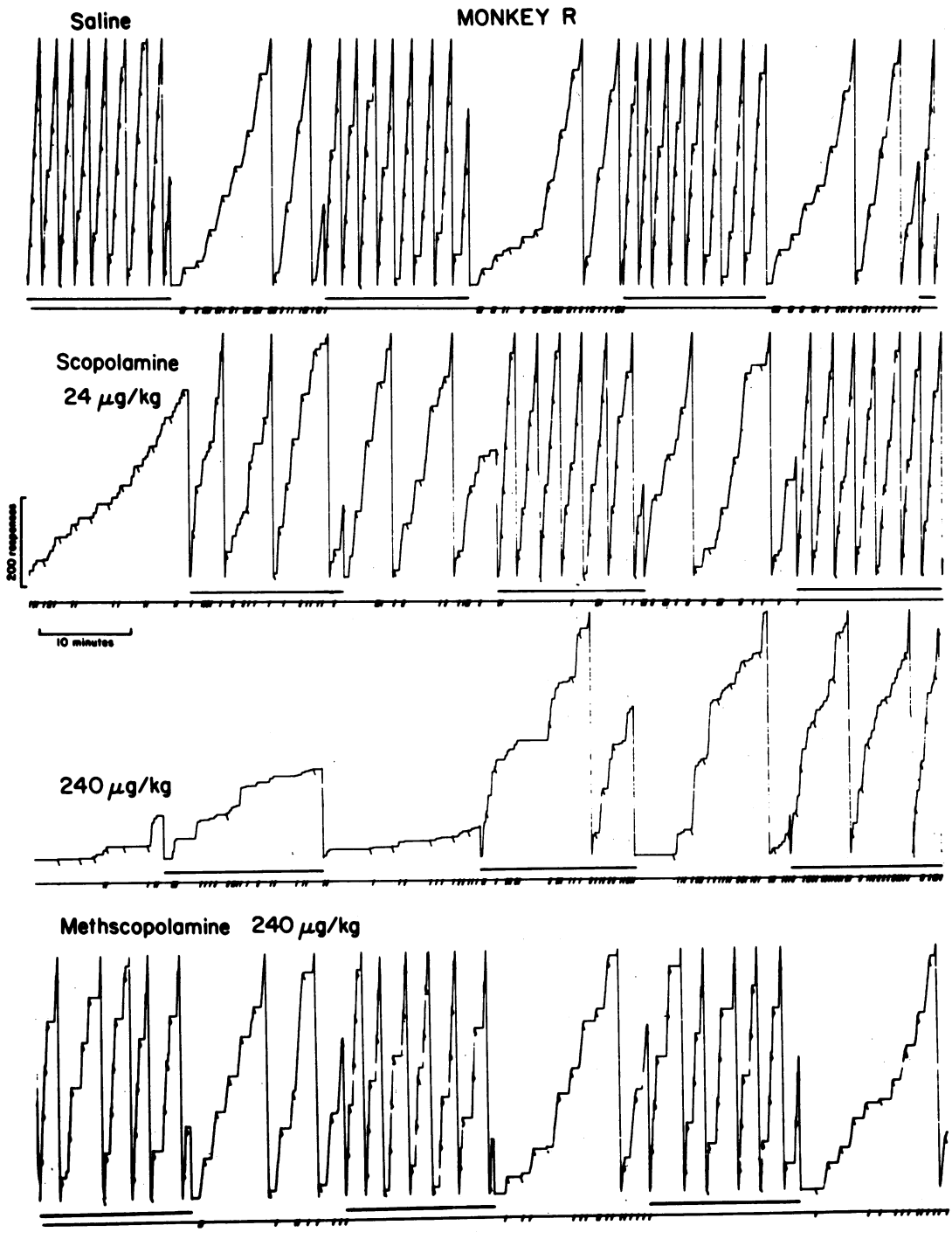

Fig. 4. Cumulative response records for Monkey R for saline, scopolamine, and methscopolamine sessions under the mult FR FI schedule. The first 90 min of the session for the 2 scopolamine records have been omitted because the response rate was virtually zero. The first 100 min of the saline and methscopolamine sessions are shown. The recording details are the same as in Figure 2.

scopolamine under the FI schedule are also generally consistent with those previously reported (e.g., Herrnstein, 1958; Laties & Weiss, 1966), though small rate-increasing effects have also been reported to occur at low doses (e.g., Boren & Navarro, 1959). Though localized rate-increasing effects were obtained in the present study, methamphetamine only decreased overall response rate in the FI component of the multiple schedule. That the overall FI response rate was not increased at any dose is in contrast to the frequently reported finding that low doses of amphetamine increase the overall response rate under an FI schedule (see review by McKearney & Barrett, 1978). There have, however, been other reports of a monotonic decrease in overall FI rate with increasing doses of amphetamine (e.g., Brown & Seiden, 1975; Evans, Ghiselli, & Patton, 1973; Harris, Snell, & Loh, 1978a, b; Heffner, Drawbaugh, & Zigmond, 1974; Stinnette & Isaac, 1975). In each of these instances where amphetamine decreased the overall rate, the FI value was relatively short (e.g., 120 sec or less). On the other hand, overall rate-increasing effects of amphetamine have also been reported with short FI durations (e.g., Branch & Gollub, 1974; de Oliveira & Graeff, 1972; McKearney, 1968; McMillan, 1969). Furthermore, the nature of the effect does not seem to depend on the overall control rate of responding since both increases and decreases have been reported with comparable control rates (e.g., see subjects R-4 and R-5 in Figure 1 of Schuster, Dockens, & Woods, 1966). Further investigation of amphetamine's effects on behavior under short FI schedules would seem necessary in order to determine the circumstances under which either increases or decreases in overall response rate may be expected.

Lyon and Robbins (1975) have suggested that, under certain circumstances, amphetamine may produce stereotypy in operant behavior. Examples of stereotyped operant behavior may include "error perseveration" (e.g., Thompson, 1977) or, in the present study, a decrease in the variability of response location. For example, it might be expected that at high doses, amphetamine would decrease switching in the FI schedule without affecting switching in the FR schedule. The effects which were obtained at the higher doses (.4 and .5 mg/kg) of methamphetamine do not seem to support this notion. Generally, with increasing doses, both methamphetamine and scopolamine increased variability of response location in each component of the multiple schedule. Admittedly, there could have been a very stereotyped pattern of responding involving only two levers that would yield a high percentage of switches. Although switches between particular levers were not recorded separately, such stereotyped switching was not evident when the subjects were observed during the drug sessions. Rather, switching occurred between all six levers in no particular pattern.

Under baseline conditions, the FR schedule generated a high rate of responding and a low level of switching, whereas the FI schedule generated a low rate of responding and a high level of switching. Boren et al. (1978) suggested that variability of response location is determined by the particular characteristics of the reinforcement schedule rather than the intermittence of reinforcement. They found that when the rate of reinforcement was equated, FR schedules generated a low degree of variability while FI schedules generated a high degree of variability.

One characteristic difference between the two schedules is the rate of responding. It could be argued that variability of response location is simply determined by the rate of responding, with low overall rates generating a high degree of variability and high overall rates generating a low degree of variability. The present drug data do not seem to support this interpretation since substantial decreases in response rate without increased switching were produced at certain doses by both methamphetamine and scopolamine. Whether variability of response location would have decreased as overall rate of responding increased in the FI schedule is unknown since only isolated instances of localized rate-increasing effects were found (during which switching still occurred). Moreover, the control levels of switching during the FI schedule would have made all but the most extreme decreases in variability difficult to detect.

Another difference between the two schedules might be the likelihood of superstitious behavior developing. Under an FI schedule, reinforcement is dependent only on the passage of time plus one response. Switching under the FI schedule was sometimes closely followed by food presentation even though a

switch was not required for reinforcement. Such adventitious reinforcement of switching may account for the observed variability of response location. Under the FR schedule, however, the characteristic "cohesive" chaining of responses (Mechner, 1958; Weiss & Gott, 1972) would make the development of superstitious behavior less likely.

In Monkeys S and E, switching under the FI schedule decreased from the high levels in the Boren et al. (1978) study to the much lower levels in the present study. The present results may be due in part to the use of a multiple schedule with an FR component. Boren et al. reported that variability under an FI schedule was much lower when that schedule was preceded by exposure to FR schedules than when it was preceded by exposure to FI schedules. Similarly, in the present study, the FR component of the multiple schedule may have influenced the level of variability in the FI component. In addition, the gradual decrease in switching over time may be an example of the characteristic "drift" in superstitious behavior (cf. Herrnstein, 1966; Skinner, 1948). If so, the present results may contribute to our understanding of superstitious behavior by showing how it was influenced by the schedule of reinforcement and by drug administration.

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